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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
10/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,193	NEYSES, LUDWIG	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2010 and 20 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23 and 25* is/are rejected.

7)☒ Claim(s) *24 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continuation Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/10/10 has been entered.

Response to Arguments

This Office Action is in response to the amendment submitted on 09/10/10. Claims 14-26 are currently pending in the application, with claims 1-13 having being cancelled. Accordingly, claims 14-26 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

1. Applicant's argument with respect to the 103(a) rejection over Chaudhary in view of Wennemuth has been fully considered. Applicant argues that claim 14 as presently amended is drawn to a method of achieving a contraceptive effect that comprises administering an inhibitor directed against a plasma membrane calcium ATPase-4 (PMCA4) isoform, which is expressed in the cell and wherein administration of such

inhibitor results in inhibition of sperm mobility and thus a contraceptive effect. Additionally, applicant argues that claim 14 makes clear that the inhibitor acts on PMCA4 pumps that are present in sperm cells and thus Chaudhary fails to supply the necessary skills to one skilled in the art with key technical teachings in order to practice the instant invention. Such arguments are however not found persuasive as the Examiner contends that applicant is arguing the newly amended claims (i.e. claim 14). It is noted that the features upon which applicant relies (i.e., that is expressed in a sperm cell and such that fertilization of an egg cannot take place) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Nonetheless, the Examiner continues to maintain that Chaudhary in view of Wennemuth still render obvious the presently amended claims.

Chaudhary teaches that plasma membrane pumps are present in all mammalian cells (i.e. any type of mammalian cell including sperm cells, erythrocytes, etc..). Additionally, Chaudhary teaches that PM Ca2+ pumps are encoded by four PMCA genes that are alternatively spliced into PMCA1, PMCA2, PMCA3, and PMCA4 with PMCA1b being the most widely expressed. While their sequences are conserved, Chaudhary teaches that the first putative extracellular domain is not. However, when Chaudhary conducted his experiments PMCA4 only differed from PMCA1b by one residue, i.e. the difference between the two is only a single residue difference. Importantly, Chaudhary teaches that Caloxin 2A1 was able to inhibit PMCA1b but also

produced a complete inhibition of plasma membrane ATPase in erythrocytes that expresses mainly PMCA4. As a result, Chaudhary suggests that Caloxin 2A1 would also inhibit all of the PMCA isoforms. While applicant argues that Chaudhary stated that inhibition of all of PMCA isoforms remain to be established, the Examiner maintains that given the disclosure of Chaudhary, one of ordinary skill in the art would have still found it obvious to try Caloxin 2A1 to inhibit PMCA4 given that Chaudhary tested Caloxin 2A1 against PMCA1b and found it to inhibit such isoform and given that PMCA1b and PMCA4 share similar sequences and PMCA4 is known to be generally expressed in all cells, and in view of the fact that Caloxin 2A1 was found to be effective against ghost erythrocytes that possess mainly PMCA4 CA2+ pumps. As a result, the Examiner maintains that one skilled in the art would have found it obvious to try Caloxin 2A1 in sperm cells and would have had a reasonable expectation of success since Caloxin 2A1 was effective in PMCA4 expressing erythrocytes.

As for applicant's arguments that Caloxin 2A1 inhibition of PMCA in different cell types is inconsistent, such arguments are not found persuasive as the lack of effect of Caloxin 2A1 in skeletal muscle is moot since Chaudhary did not explicitly state that skeletal muscles possess PMCA4 expression. On the other hand, Chaudhary explicitly states that Caloxin 2A1 was effective on erythrocyte ghost cells that express mainly PMCA4 thus suggesting to one skilled in the art that Caloxin 2A1 is inhibiting the PMCA4 isoform expressed in that cell type. If such technical reasoning is false, it is incumbent upon applicant to demonstrate that Caloxin 2A1 does not in fact bind to PMCA4 in erythrocytes but rather to another type of calcium pump. However, absent

evidence from applicant, the Examiner asserts that Caloxin 2A1 is in fact effective in inhibiting PMCA4 and thus should also be effective against the PMCA4 pumps that are expressed in sperm cells.

Again, the Examiner reiterates all the previous arguments from the previous Office action regarding Wennemuth and maintains that Chaudhary in view of Wennemuth still render obvious applicant's invention. As for applicant's argument Wennemuth teaches that PMCA an NCX CA2+ pumps act in synergy and PMCA is not solely responsible for Ca2+ clearance, the Examiner again disagrees and incorporates by reference the previous arguments regarding Wennemuth from the previous office Action. Additionally, the Examiner refers applicant to Wennemuth who clearly teaches that it was found that the Ca2+ ATPase pump of the plasma membrane (abbreviated by Wennemuth as PMCA) performs the major task of Ca2+ clearance (see abstract). While NCX may also be involved Wennemuth explicitly implicated PMCA4 as the major Ca2+ pump in mouse sperms. In fact, Wennemuth tested the inhibition of both types of pumps (NCX and PMCA) by raising the pH and found that PMCA was inhibited to a higher extent than NCX further supporting the results of Wennemuth that PMCA performs the major task of Ca2+ clearance in sperm cells (see pg. 120). Consequently, based on the disclosure of Wennemuth the Examiner maintains that PMCA is the major pump in sperm cells and thus obvious to inhibit since inhibition of the pump leads to reduction in motility and reduction in motility of sperm cells would reduce the ability of the sperm cell to fertilize an egg.

As for applicant's argument that Wennemuth did not demonstrate localization of PMCA to the acrosomal portions while applicant has demonstrated localization of PMCA to both the tail and acrosomal portions of both murine and human sperm, such arguments are not found persuasive as motility hinges on the movement of the tail. Since Wennemuth demonstrated PMCA in the tail and inhibition of motility by inhibiting PMCA with the Caloxin 2A1 molecule of Chaudhary would prevent motility of the sperm and therefore obvious to one skilled in the art that the sperm would not be able to undergo sperm capacitation (i.e. undergo hypermotility) or reach the egg in order for acrosomal reaction to occur.

As for applicant's argument that Chaudhary did not test sperm cells and that Chaudhary taught that Caloxin 2A1 had tissue-specific effect, the Examiner maintains that erythrocytes which contained PMCA4 were tested and found to be inhibited by Caloxin 2A1. Chaudhary further teach that PMCA (i.e. inclusive of PMCA4) are expressed in all cells (i.e. inclusive of sperm cells). Additionally, Wennemuth demonstrated the presence of PMCA in sperm cells. Consequently, the Examiner asserts that it would have been obvious to one skilled in the art to try Caloxin 2A1 or carboxyeosin to block PMCA4 in light of the disclosure of Chaudhary and Wennemuth. While applicant demonstrated the localization of PMCA4 in the acrosomal portion of the sperm cell, this in no way negates the prima facie case of obviousness established by Chaudhary and Wennemuth. For the foregoing reasons, the Examiner maintains that the rejection of claims 14-15 and 17-20 over Chaudhary in view of Wennemuth was indeed proper.

2. Applicant's argument with respect to the rejection of claims 21-22 has been fully considered. Applicant argues that Chaudhary and Wennemuth do not provide the skilled person a finite set of solutions, predictability and reasonable expectation of success in achieving the claimed contraceptive method. Such arguments are not found persuasive as the Examiner maintains that Chaudhary in view of Wennemuth did indeed render obvious applicant's invention with the disclosure of Chaudhary who teach that Caloxin 2A1 is an effective PMCA4 inhibitor and Wennemuth who teaches that PMCA is localized to the tail of sperm cells that the ester form of carboxyeosin could be used to block the inhibitor and thus motility of the sperm cell. Zimmerman was provided to demonstrate that oral contraceptives are known to be administered in various forms and thus would have been well within the purview of the skilled artisan to formulate the PMCA4 inhibitor in oral, parenteral, or coated mechanical contraceptive form. As for Papurt, it was provided to demonstrate that condoms are contraceptive devices well known in the art as mechanical barriers. Thus, to enhance contraceptive effects and prevent infections, one of ordinary skill in the art would have indeed found it obvious to add the use of condoms in the aforementioned contraceptive method with the reasonable expectation of obtaining a method that is effective in preventing conception and effective in reducing infections.

For the foregoing reasons, the rejections of record were indeed proper. However, in view of applicant's amendment, the following objection, 112, second paragraph, 102(b) and modified 103 (a) Non-Final rejections are being made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited).

It is respectfully pointed out that the recitation "a contraceptive composition" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robbie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Chaudhary et al. teach that plasma membrane (PM) Ca2+ pump is a Ca2+ Mg2+-ATPase that expels Ca2+ from cells to help them maintain low concentrations of cytosolic Ca2+ (see abstract). Additionally, Chaudhary et al. teach that the PM calcium pumps use the energy of hydrolysis of ATP to expel cellular Ca2+ (see pg. C1027, left

col., Introduction section). Moreover, Chaudhary et al. teach that the PM Ca2+ pumps are present in all mammalian cells (i.e. inclusive of sperm cells) thereby suggesting that such pumps are also present in humans as well (see pg. C1027, left col., Introduction Section). Specifically, Chaudhary et al. teach that PM Ca2+ pumps are encoded by four PM Ca2+-ATPase genes (a.k.a. PMCA) whose sequences are conserved in the various isoforms (pg. C1027, right col.). Furthermore, Chaudhary et al. teach that the sequence of extracellular domain 401-413 in human PMCA1b is similar to the corresponding sequences in PMCA 4 and thus supporting the notion that the PMCA inhibitor of Chaudhary et al. should also inhibit PMCA4 (see pg. C1029, left col. Discussion Section, last paragraph). Particularly, Chaudhary et al. teach Caloxin 2A1 as a novel PM Ca2+ pump inhibitor selected for biding to the extracellular domain of PMCA (see abstract and pg. C1029, right col., paragraph 1). Chaudhary et al. teach that Caloxin 2A1 was dissolved in Krebs solution (i.e. carrier) which contains 115 mM NaCl, 5 mM KCl, 22 mM NaHC93, 1.7 mM CaCl2, 1.1 mM MgCl2, 1.1 kH2Po4, 0.3 mM EDTA, and 7.7 mM glucose (instant claim 20; see pg. C1028, left col., Contractility experiments, last paragraph).

Accordingly, the teachings of Chaudhary et al. anticipate claim 2.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited) as applied to claim 20 above and in further view of Pasquale (U.S. 4,066,757).

The Chaudhary reference is as discussed above and incorporated by reference herein. However, Chaudhary does not teach addition of a conventional contraceptive.

Pasquale teaches an oral contraceptive regimen wherein progestin is administered from the fifth through the twenty-fifth day of the physiological cycle (see abstract). Importantly, Pasquale teaches that progestational agents which are effective in conventional contraceptive preparations are generally administered in amounts less than 1 mg to up to 25 mg per day depending upon their potency (see col. 3, lines 1-25).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to further add the progestational agent of Pasquale since Pasquale teaches that progestational agents can lead to high contraceptive effect. Thus, given the teachings of Chaudhary and Pasquale, one of ordinary skill would have been motivated to add progestational agents to the composition of Chaudhary with the reasonable expectation of providing an enhanced contraceptive composition that is also effective in inhibiting sperm.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **(see M.P.E.P 608.01 (k))**.

Claim 22 is particularly vague and indefinite given that applicant is claiming a contraceptive composition further comprising a condom **(in sentences 2 of claim 22)**. It is unclear to the Examiner how the composition comprises or contains a condom. Given that applicant did not particularly point out how such composition can contain a contraceptive device, one of ordinary skill in the art would not be able to fully ascertain the metes and bounds of the aforementioned claim.

As a result of the above inconsistencies, the aforementioned claim is unable to be examined as disclosed given that the scope of the claimed subject matter would not be able to be determined by one of ordinary skill in the art

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-15 and 17-19 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128, previously cited).

Chaudhary et al. teach that plasma membrane (PM) Ca2+ pump is a Ca2+ Mg2+-ATPase that expels Ca2+ from cells to help them maintain low concentrations of cytosolic Ca2+ (see abstract). Additionally, Chaudhary et al. teach that the PM calcium pumps use the energy of hydrolysis of ATP to expel cellular Ca2+ (see pg. C1027, left col., Introduction section). Moreover, Chaudhary et al. teach that the PM Ca2+ pumps are present in all mammalian cells (i.e. inclusive of sperm cells) thereby suggesting that such pumps are also present in humans as well (see pg. C1027, left col., Introduction Section and pg. C1029, right col., last col.). Specifically, Chaudhary et al. teach that PM Ca2+ pumps are encoded by four PM Ca2+-ATPase genes (a.k.a. PMCA) whose sequences are conserved in the various isoforms (pg. C1027, right col.). Furthermore, Chaudhary et al. teach that the sequence of extracellular domain 401-413 in human PMCA1b is similar to the corresponding sequences in PMCA 4 and thus supporting the notion that the PMCA inhibitor of Chaudhary et al. should also inhibit PMCA4 (see pg. C1029, left col. Discussion Section, last paragraph). Particularly, Chaudhary et al. teach Caloxin 2A1 as a novel PM Ca2+ pump inhibitor selected for biding to the extracellular domain of PMCA (see abstract and pg. C1029, right col., paragraph 1). Chaudhary et al. teach that Caloxin 2A1 was dissolved in Krebs solution (i.e. carrier)

which contains 115 mM NaCl, 5 mM KCl, 22 mM NaHC93, 1.7 mM CaCl2, 1.1 mM MgCl2, 1.1 kH2Po4, 0.3 mM EDTA, and 7.7 mM glucose (instant claim 20; see pg. C1028, left col., Contractility experiments, last paragraph). In fact, Chaudhary et al. teach that Caloxin 2A1 was able to bind PMACA1 and produced a complete inhibition of PM Ca2+ pumps in erythrocytes that mainly express PMCA4 (see pg. C1029, left col., Discussion Section, paragraph 4). Consequently, Chaudhary suggests that Caloxin 2A1 would inhibit all of the PMCA isoforms (see pg. C1029, left col., Discussion Section, paragraph 4).

Chaudhary et al. however do not specifically teach a method achieving contraceptive effect comprising a PMCA4 isoform inhibitor. Likewise, Chaudhary et al. do not teach that the PMCA4 inhibitor is performed as a single contraceptive event or as a repeated contraceptive event in sperm cells.

Wennemuth et al. teach that the spermatozoon is specialized for a single vital role in fertilization (see abstract). In fact, past studies show that Ca2+ signals produced by the opening of PM membrane channels initiate several events required for the sperm to reach and enter the egg but reveal little about how resting Ca2+ is maintained or restored after elevation (see abstract). This suggests that blocking such PM channels should prevent fertilization as inhibition of such PM channels would prevent the sperm from reaching the egg and thereby block fertilization. Additionally, Wennemuth et al. teach that like other excitable cells, mammalian spermatozoa (i.e. including human

sperm; instant claims 18-19) possess multiple voltage-gated calcium channels and use Ca2+ signals to control physiological responses (see pg. 115, left col., Introduction). Particularly, Wennemuth et al. teach that calcium is considered a regulator of sperm motility, a participant in capacitation, and an essential second messenger for the acrosome reaction (i.e. a reaction that occurs when sperm is penetrating the layers of the oocyte during fertilization; see pg. 115, left col.). According to Wennemuth et al., the sperm PM depolarizes, Ca2+ channels open, Ca2+ enters, and the Ca2+-dependent acrosome reaction ensues (see pg. 115, left col.). Wennemuth et al. teach that four major Ca2+ clearance mechanisms exist in most animal cells including PMCA which exports cytoplasmic Ca2+ ion and imports one or two extracellular protons at the expense of ATP (see pg. 115, right col., paragraph 2). Importantly, Wennemuth et al. teach that the Ca2+ ATPase pump of the PM (PMCA) performs the major task of Ca2+ clearance (see abstract and pg. 120, right col., last paragraph). Additionally, Wennemuth et al. teach that carboxyeosin (instant claim 15) was used in blocking PMCA in sperm cells but prevented the cells from KCL depolarization (see pg. 120, right col., top paragraph). Thus, inhibition of PMCA would necessarily result in a contraceptive effect as the acrosome reaction (i.e. sperm penetrating the egg or ovum) would necessarily be prevented (instant claim 14) by inhibition of PMCA.

As for the administration of the aforementioned PMCA4 inhibitor as a single contraceptive event or as a repeated contraceptive event in sperm cells, the Examiner maintains that it would have been obvious to one skilled in the art during routine

experimentation to either administer a single dosage of such inhibitor or repeated doses depending on the desired regimen or the patient population to be treated.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize Caloxin 2A1 to inhibit PMCA4 in sperm PM since Wennemuth et al. teach that the Ca2+ PM pump is involved in the fertilization of human eggs by sperms and given that Wennemuth teaches that PMCA is localized in the tail of mammalian sperms. Moreover, one of ordinary skill in the art would have found it obvious to utilize the PMCA4 inhibitor Caloxin 2A1 as either a single contraceptive event or as a repeated contraceptive event depending on the desired regimen or patient to be treated. Thus, given the teachings of Chaudhary and Wennemuth, one of ordinary skill would have been motivated to utilize Caloxin 2A1 to inhibit PMCA4 inhibitor in sperm cells with the reasonable expectation of providing a method that is effective in preventing conception and effective in inhibiting fertilization.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128, previously cited) as applied to claims 14-15 and 17-19 above and in further view of Zimmerman et al. (U.S. 2002/0164368, previously cited).

The Chaudhary and Wennemuth references are as discussed above and incorporated by reference herein. However, Chaudhary and Wennemuth do not teach oral, parenteral or coated mechanical contraceptive of the PMCA inhibitors.

Zimmerman teaches male contraceptive composition that can be administered orally (see abstract). Zimmerman also teaches that oral contraceptives are the most prominent chemical contraceptive agents; however, other chemical agents can be used in the form of creams, foams, gels and suppositories (see pg. 1, paragraphs 0003 and 0008). Of interest, Zimmerman demonstrated that contraceptive compositions can be made in various forms including oral, parenteral, or topical administration (see pg. 5, paragraphs 0060-0062).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the PMCA4 inhibitor composition of Chaudhary in various forms since Zimmerman teaches that contraceptive compositions can be formulated as an oral, parenteral or topical application. Thus, given the teachings of Chaudhary, Wennemuth, and Zimmerman, one of ordinary skill would have been motivated to formulate the composition of the aforementioned method as an oral, parenteral, or topical formulation in view of the disclosure of Zimmerman with the reasonable expectation of providing a contraceptive method that can be easily administered.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128, previously cited) as applied to claims 14-15 and 17-19 above and in further view of Perloe et al. (The formula of Male Fertility, Published online February 2002, pgs. 1-9).

The Chaudhary and Wennemuth references are as discussed above and incorporated by reference herein. Chaudhary and Wennemuth however do not specifically teach a method for diagnosing infertility in a human male.

The Examiner however maintains that it is routine in the art to obtain a biological sample. In fact, Perloe et al. teach that when diagnosing male fertility a semen sample is typically collected from the male in a sterile container (see pg. 2). Subsequently, a semen analysis is typically performed to examine consistency of the sperm and determine the presence of infections (see pg. 1-2).

Though, Perloe does not teach detection of a mutation in the PMCA4 gene encoding PMCA4 isoform, the Examiner maintains that given that Chaudhary in view of Wennemuth suggests that PMCA4 is involved in cell motility and affects sperm capacitation, acrosomal reaction and thus conception, the converse should also be true, i.e., inhibition of the normal functioning of such channel (i.e. PMCA4) should prevent

conception from occurring. Consequently, one of ordinary skill in the art would have found it obvious during infertility diagnosis to examine the biological sample for mutations or polymorphisms in the PMCA4 gene since the non-mutated gene product (i.e. the normal PMCA4 isoform) is suggested by the prior art to be involved in conception.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to obtain a sample of semen and analyze such semen during fertility determination and further test for PMCA4 mutation since Chaudhary in view of Wennemuth suggests that PMCA4 is involved in conception. Thus, given the teachings of Chaudhary, Wennemuth, and Perloe, one of ordinary skill would have been motivated diagnose male infertility via testing of PMCA4 gene mutation with the reasonable expectation of providing a diagnostic method that is effective in determining male infertility.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030, previously cited) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128, previously cited) as applied to claims 14-15 and 17-19 above and in further view of Perloe et al. (The formula of Male Fertility, Published online February 2002, pgs. 1-9) and Burnett et al. (Toxicology, 1997, Vol. 119, pgs. 83-93).

The Chaudhary, Wennemuth, and Perloe references are as discussed above and incorporated by reference herein. However, Chaudhary, Wennemuth, and Perloe do not specifically teach detection of the PMCA4 isoform is performed using immunohistochemistry.

Burnett et al. teach that immunohistochemistry has been used as a tool in all aspects of biological materials (see pg. 83, right col., last paragraph and pg. 84, left col., top paragraph). Such method uses the basic concepts of using an antibody directed against an antigenic component in a tissue, together with a method of visualizing this complex and that depending on the type of immunohistochemistry used different response magnification can be obtained (see pg. 84, left col., last paragraph, right col., top paragraph, and fig. 1).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize immunohistochemistry techniques in the biological semen sample to detect the amount of PMCA4 protein expression in such sperms since decreased expression would signify low motility and thus low probability for conception. Thus, given the teachings of Chaudhary, Wennemuth, Perloe, and Burnett, one of ordinary skill would have been motivated to utilize immunohistochemistry in view of the disclosure of Burnett with the reasonable expectation of detecting the amount of protein expression in sperm samples.

Objections

Claims 24 and 26 are objected to because of the following informalities: Claims are dependent upon a rejected claim. Applicant is required to incorporate all of the limitations of claims 14 and 23 into the aforementioned claims. Appropriate correction is required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/S. J. L./

Examiner, Art Unit 1627

09/30/2010

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